CLAIMS

1. A preventive and/or therapeutic agent for spinal canal stenosis, which comprises an aldose reductase inhibitory compound.

2. The preventive and/or therapeutic agent for spinal canal stenosis according to claim 1, wherein the spinal canal stenosis is cervical spinal canal stenosis, thoracic spinal canal stenosis, lumbar spinal canal stenosis or wide spinal canal stenosis.

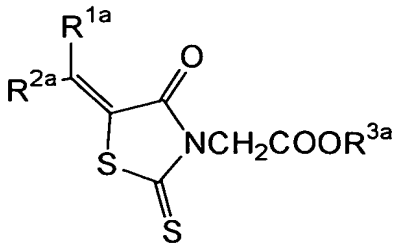
3. The preventive and/or therapeutic agent for spinal canal stenosis according to claim 1, wherein the agent is used for improving paralysis, hypoesthesia, pain or numbness.

4. The preventive and/or therapeutic agent for spinal canal stenosis according to claim 1, wherein the agent is used for improving physical ability.

5. The preventive and/or therapeutic agent for spinal canal stenosis according to claim 4, wherein the agent for improving physical ability is used for improving reduction of muscle power, intermittent claudication and gait disability.

6. The preventive and/or therapeutic agent for spinal canal stenosis according to claim 1, wherein the agent is used for improving dysuria or dyschezia.

7. The preventive and/or therapeutic agent for spinal canal stenosis according to claim 1, wherein the aldose reductase inhibitory compound is represented by formula (I):



(I)

wherein

1) R^{1a} and R^{2a} are the same or different and each represents phenyl which may be substituted by at least one group selected from the following (1)-(10):

(1) halogen,

(2) trifluoromethyl,

(3) hydroxyl,

(4) nitro,

(5) carboxyl,

(6) amino which may be substituted by C1-4 alkyl,

(7) C1-4 alkyl, alkoxy or alkylthio,

(8) phenyl,

(9) a heterocyclic group containing at least one atom selected from a nitrogen atom, a sulfur atom and an oxygen atom, which may be substituted by at least one group selected from (a) halogen, (b) trifluoromethyl, (c) phenyl, (d) nitro, (e) hydroxyl, (f) carboxyl, (g) amino which may be substituted by C1-4 alkyl, (h) C1-4 alkyl, (j) C1-4 alkoxy, and (k) C1-4 alkylthio, or

(10) C1-4 alkyl substituted by at least one substituent selected from hydroxyl, phenyl, and the heterocyclic group described above (9),

2) R^{1a} is hydrogen and R^{2a} is the following (1)-(6):

(1) C4-7 cycloalkyl or cycloalkenyl which may be substituted by at least one C1-4 alkyl,

(2) anthryl or naphthyl,

(3) phenyl which may be substituted by at least one group selected from the following (a)-(k):

(a) halogen,

(b) trifluoromethyl,

(c) hydroxyl,

(d) nitro,

(e) carboxyl,

(f) amino which may be substituted by C1-4 alkyl,

(g) C1-4 alkyl, alkoxy or alkylthio,

(h) phenyl,

(j) a heterocyclic group containing at least one atom selected from a nitrogen atom, a sulfur atom and an oxygen atom, which may be substituted by at least one group selected from (i) halogen, (ii) trifluoromethyl, (iii) phenyl, (iv) nitro, (v) hydroxyl, (vi) carboxyl, (vii) amino which may be substituted by C1-4 alkyl, (viii) C1-4 alkyl, (ix) C1-4 alkoxy, and (x) C1-4 alkylthio,

(k) C1-4 alkyl substituted by at least one substituent selected from hydroxyl, phenyl, and the heterocyclic group described above (j),

(4) a heterocyclic group containing at least one atom selected from a nitrogen atom, a sulfur atom and an oxygen atom, which may be substituted by at least one group selected from the following (a)-(k):

(a) halogen,

(b) trifluoromethyl,

(c) phenyl,

(d) nitro,

(e) hydroxyl,

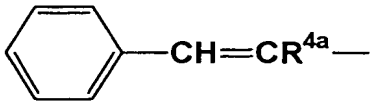
(f) carboxyl,

(g) amino which may be substituted by C1-4 alkyl,

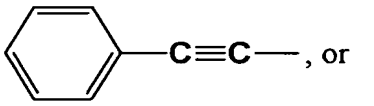
(h) C1-4 alkyl, alkoxy or alkylthio,

(j) oxo, or

(k) C1-4 alkyl substituted by at least one substituent selected from hydroxyl, phenyl, and the heterocyclic group described above (j) in (3),

(5) 

wherein R^{4a} is hydrogen or C1-4 alkyl, or

(6)  , or

3) R^{1a} taken together with R^{2a} is tetramethylene or pentamethlene;

R^{3a} is

(1) hydrogen,

(2) C1-12 alkyl,

(3) C7-13 aralkyl,

(4) C4-7 cycloalkyl or cycloalkenyl which may be substituted by at least one C1-4 alkyl,

(5) phenyl which may be substituted by at least one group selected from the following (a)-(k):

(a) halogen,

(b) trifluoromethyl,

(c) hydroxyl,

(d) nitro,

(e) carboxyl,

(f) amino which may be substituted by C1-4 alkyl,

(g) alkoxy or alkythio which may be substituted by C1-4 alkyl,

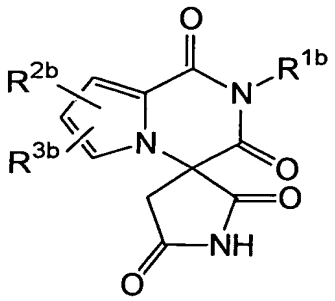
(h) phenyl,

(j) a heterocyclic group containing at least one atom selected from a nitrogen atom, a sulfur atom and an oxygen atom, which may be substituted by at least one group selected from (i) halogen, (ii) trifluoromethyl, (iii) phenyl, (iv) nitro, (v) hydroxyl, (vi) carboxyl, (vii) amino which may be substituted by C1-4 alkyl, (viii) C1-4 alkyl, (ix) C1-4 alkoxy, and (x) C1-4 alkylthio, and,

(k) C1-4 alkyl substituted by at least one substituent selected from hydroxyl, phenyl, and the heterocyclic group described above (j), or

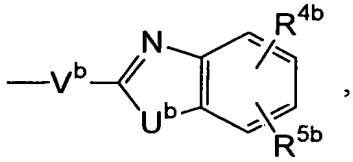
a salt of acid thereof when R^{3a} represents hydrogen, or a solvate thereof.

8. The preventive and/or therapeutic agent for spinal canal stenosis according to claim 1, wherein the aldose reductase inhibitory compound is a compound represented by formula (II):



(II)

wherein R^{1b} represents (1) hydrogen, (2) lower alkyl, (3) substituted or unsubstituted aryl(lower alkyl), (4) substituted or unsubstituted aryl, or (5)



,

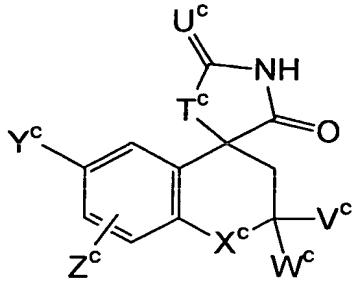
wherein R^{4b} and R^{5b} are the same or different and each represents (a) hydrogen, (b) halogen, (c) trifluoromethyl, (d) lower alkyl, (e) lower alkoxy, (f) acyl, (g) nitro, (h) amino, (i) lower alkylamino, or (j) di(lower alkyl)amino; U^b represents (a)

oxygen, (b) sulfur, or (c) $-NR^{6b}-$ wherein NR^{6b} represents hydrogen or lower alkyl, and V^b represents lower alkyl;

wherein R^{2b} and R^{3b} are the same or different and each represents (1) hydrogen, (2) halogen, (3) lower alkyl, (4) lower alkoxy, (5) acyl, (6) nitro, (7) amino, (8) lower alkylamino, (9) di(lower alkyl)amino, (10) allyl or (11) allyl which is substituted by lower alkyl, lower alkoxy or acyl, or

a salt thereof or a solvate thereof;

a compound represented by formula (III):



(III)

wherein T^c represents sulfur or NH;

U^c represents oxygen, sulfur or imino;

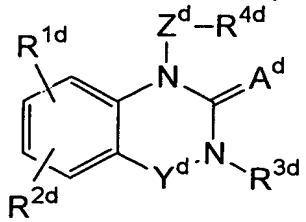
one of V^c and W^c represents hydrogen; halogenomethyl; 1H-tetrozol-5-yl; $-COOR^c$ wherein R^c is hydrogen, alkyl, $-(CH_2CH_2O)_nCH_3$ wherein n is an integer of 1 to 113, or substituted phenyl; $—CON\begin{matrix}R^{1c}\\ \diagdown\\ R^{2c}\end{matrix}$ wherein R^{1c} and R^{2c} are the same or different and each represents hydrogen, alkyl, $-(CH_2CH_2O)_nCH_3$ wherein n is an integer of 1 to 113; or substituted phenyl; $-CH_2OR^{3c}$ wherein R^{3c} is hydrogen or alkyl; or $—CH_2N\begin{matrix}R^{4c}\\ \diagdown\\ R^{5c}\end{matrix}$ wherein R^{4c} and R^{5c} are the same or different and each represents hydrogen or alkyl, and the other represents hydrogen or alkyl;

X^c represents oxygen or sulfur;

Y^c and Z^c are the same or different and each represents hydrogen, halogen, alkyl, alkoxy, or alkylthio, or

a salt thereof or a solvate thereof; or

a compound represented by formula (IV):



(IV)

wherein R^{1d} and R^{2d} are the same or different and each represents hydrogen, halogen, lower alkoxy, or halo(lower alkyl);

R^{3d} represents (1) aryl or aryl(lower alkyl) which may be substituted, or (2) heterocyclic ring-(lower alkyl);

R^{4d} represents carboxy or protected carboxy;

A^d represents oxygen or sulfur;

Y^d represents carbonyl, thiocarbonyl, or sulfonyl;

Z^d represents lower alkylene, or

a salt thereof or a solvate thereof.

9. The preventive and/or therapeutic agent for spinal canal stenosis according to claim 7, wherein the aldose reductase inhibitory compound is 5-[(1Z,2E)-2-methylphenylpropenylidene]-4-oxo-2-thioxo-3-thiazolidine acetic acid.

10. The preventive and/or therapeutic agent for spinal canal stenosis according to claim 8, wherein the aldose reductase inhibitory compound is (R)-2-(4-bromo-2-fluorobenzyl)spiro[1,2,3,4-tetrahydropyrrolo[1,2-a]pyrazine-4,3'-pyrrolidine]-1,2',3,5'-tetrone, (2S,4S)-6-fluoro-2',5'-dioxospiro[3,4-dihydro-2H-1-benzopyran-4,4'-imidazolidine]-2-carboxamide or 2-[3-(4-bromo-2-fluorobenzyl)-7-chrolo-2,4-dioxo-1,2,3,4-tetrahydroquinazolin-1-yl]acetic acid.

11. The preventive and/or therapeutic agent for spinal canal stenosis according to claim 1, wherein the aldose reductase inhibitory compound is

(1) DL-spiro(2-fluoro-9H-fluoren-9,4'-imidazolidine)-2',5'-dione,

(2) 2,7-difluoro-4,5-dimethoxyspiro[9H-fluoren-9,4'-imidazolidine]-2',5'-dione,

(3) N-[3,5-dimethyl-4-(nitromethylsulphonyl)phenyl]-2-(2-methylphenyl)acetamide,

(4) N-(carboxymethyl)-7-fluoro-N-methyl-9-oxoxanthin-2-sulphoamide,

(5) 3-(4-methoxy-5-oxo-3-phenyl-2,5-dihydrofuran-2-yl)propanoic acid ethyl ester,

(6) 2-formamide-3-[5'-(2-formamide-1-hydroxyethyl)-2,2'-dihydroxybiphenyl-5-yl]-3-hydroxypropyonic acid,

(7) 2-[3-methyl-5-(4,5,7-trifluorobenzothiazol-2-ylmethyl)-phenyl]acetic acid,

(8) 2-[5-fluoro-2-[N-(3-nitrobenzyl)thiocarbamoyl]phenoxyacetic acid,

(9) 8'-chrolo-2',3'-dihydrospiro[pyrrolidine-(3,6')(5'H)-pyrro[1,2,3-de][1,4]benzoxazine]-2,5,5'-trione,

(10) 2-[1-(3,4-dichrolobenzyl)-2,4-dioxo-1,2,3,4-tetrahydroquinazolin-3-yl]acetic acid,

(11) 2-[4-(4,5,7-trifluorenzothiazol-2-yl)methyl-3-oxo-3,4-dihydro-2H-1,4-benzothiazin-2-yl]acetic acid,

(12) 1-(benzo[b]thiophen-2-ylsulphonyl)hydantoin,

(13) 1-(3-bromobenzo[b]furan-2-ylsulphonyl)hydanthione,

(14) 3-(carboxymethyl)-1-(3-nitrobenzyl) parabanic acid,

(15) 1',3'-bis(acetoxymethyl)spiro[fluoren-9,4'-imidazolidine]-2',5'-dione,

(16) 2,8-diisopropyl-3-thioxo-3,4-dihydro-2H-1,4-benzoxazine-4-acetic acid,

(17) N-[5-(trifluoromethyl)-6-methoxy-1-naphthalenyl]thioxomethyl]-N-methylglycine),

(18) (2,6-dimethylphenylsulphonyl)nitromethane,

(19) N-[4-(2,4-dioxothiazolidin-5-ylmethyl)phenyl]-1-phenyl-cyclopropane-1-carboxamide,

(20) 2-[3-oxo-4-(4,5,7-trifluorobenzothiazol-2-ylmethyl)-3,4-dihydro-2H-1,4-benzothiazin-2-yl]acetic acid,

(21) 2-[3,7-dimethylocta-2(E),6-didienyl]-2,3-epoxy-5,7-dihydroxy-6-methyl-1,2,3,4-tetrahydronaphthalene-1,4-dione,

(22) 6-fluoro-2-methylspiro[chroman-4,4'-imidazolidin]2',5'-dione,

(23) (S)-6-fluorospiro(chroman-4,4'-imidazolidine)-2',5'-dione,

(24) 3,4-dihydro-4-oxo-3-[[5-((trifluoromethyl)-2-benzothiazolyl]methyl]-1-phthalazine acetic acid,

(25) 5-(3-ethoxy-4-pentyloxyphenyl)-2,4-thiazolidinedione,

(26) 3-[(4-bromo-2-fluoro-phenyl)methyl]-3,4-dihydro-4-oxo-1-phthalazine acetic acid,

(27) ascorbyl gamolenate,

(28) ICI-10552,

(29) ICI-215918,

(30) JTT-811,

(31) lindolrestat,

(32) salfredins,

(33) TJN-732,

(34) TAT,

(35) thiazocin-A,

(36) axillarin, or

(37) minalrestat.

12. A medicine which comprises the aldose reductase inhibitory compound according to claim 1 in combination with at least one pharmaceutical agent selected from prostaglandins, prostaglandin derivatives formulations, nonsteroidal anti-inflammatory drugs, vitamin compounds, muscle relaxants, antidepressants, poly ADP-ribose polymerase inhibitors, excitatory amino acid receptor antagonists, radical scavengers, astrocyte modulators, IL-8 receptor antagonists, and immunosuppressive drugs.

13. A method for prevention and/or treatment for spinal canal stenosis, which comprises administering to a mammal an effective amount of an aldose reductase inhibitory compound.

14. Use of an aldose reductase inhibitory compound for preparation of a preventive and/or therapeutic agent for spinal canal stenosis.